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TABLE 1. Hematologic Laboratory Data

	First admission	Just before hydroxyurea therapy	Last admission
Hbg %	8.4	8.1	2
WBC/μl	94,000	370,000	33,000
Blast %	2	4	—
Promyelocyte %	5	6	4
Myelocyte %	25	10	20
Metamyelocyte %	9	2	13
Neutrophil %	30	71	32
Band %	24	4	20
Eosinophil %	—	—	10
Basophil %	—	—	1
Lymphocyte %	4	2	—
Monocyte %	1	1	—
NRBC/100	4	3	1
Platelet/μl	105,000	100,000	9,000
LAP score[a]	2		
LDH IU/L[b]	2,300		
B_{12} pg/ml[c]	827	—	—

[a]Normal range 30–100.
[b]Normal range 200–400 IU/L.
[c]Normal ragne 190–800 pg/ml.

Translocation T(4;21) Associated With the Pelger-Hüet Anomaly in a Patient With Ph Chromosome-Negative CML

To the Editor: A patient with chronic myeloproliferative disorder (MPD), most probably Ph chromosome negative chronic myelogenous leukemia (CML), is presented. The disease was associated with the Pelger-Hüet anomaly and the t(4;21)(p12;q21 or 22). More than 90% of CML patients are Ph chromosome positive (Ph^+CML). About 50% of Ph^-CML patients have a bcr/abl rearrangement (Ph^-bcr^+). The rest of the Ph^-CML are Ph^-bcr^- and it is difficult to discern them from Ph^+bcr^+ merely on a clinical and morphological basis [1]. Recently 11 patients with Ph^-/bcr^- CML were reported. They were clinically and morphologically indistinguishable from those found in the typical cases of bcr^+ CML [2]. We describe a patient with clinical manifestation of Ph^-CML who had a unique t(4;21) (p12;q21 or 22) and in addition had the Pelger-Hüet anomaly.

An 81-year-old female immigrant from Russia was admitted to the Internal Medicine Department of Soroka Medical Center in November 1993 because of high fever, cough, and dyspnea. Her past history was remarkable for hysterectomy because of ectopic pregnancy in 1958, cholecystectomy for cholelithiasis in 1981, and choledocholitotomy for recurrent obstructive jaundice in 1981. Physical examination on admission revealed pallor, fever of 39°C, spleen palpable at 5 cm below the left costal margin, and hepatomegaly (4 cm below the right costal margin).

Laboratory data are shown in Table I. On peripheral blood smears all cells of myeloid origin had the Pelger-Hüet anomaly. Liver and renal function tests were normal. Bone marrow biopsy and aspiration were consistent with myeloproliferative disorder. No fibrosis was documented. All bone marrow cells showed the pelgroid nuclei. Normal karyotype was found in peripheral lymphocytes, while cytogenetic analysis of the bone marrow showed 46, XX, t(4;21) (p12;q21 or 22). A diagnosis of Ph negative CML was most likely. The patient was treated with cefuroxime for presumed infection. Later, obstructive jaundice occurred and bile stones were removed by papillotomy. After recovery, she received treatment with hydroxyurea, 1.5 g/day, and allopurinol, 600 mg/day, because of hyperleukocytosis of 370,000/μl (Table I). June 17, 1994 she was admitted again because of dizziness, multiple ecchymoses, and a blood count of 2 g%Hb, a white blood cell (WBC) count of 33,000/μl with shift to the left (Table I), and a platelet count of 9,000/μl. Lactic acidosis was documented. Despite intensive supportive therapy, the patient succumbed due to cardiac arrest. Autopsy was refused. We have no blood smears prior to admission to the hospital, and no molecular analysis could be carried out because of lack of a bone marrow specimen.

The only CML case so far reported is that by Donti et al. [3], who described a blast crisis with t(4;21) (p16;q22) in a patient previously defined as having typical CML with variant Ph t(2;9;22). However, no Pelger-Hüet anomaly was decomented, and the translocations are at variance from our case.

Acquired Pelger-Hüet anomaly, as described by Pelger, is sometimes observed in MPD, dysmyelopoietic syndromes, severe infections, and in other clinical entities such as Hodgkin Disease, non-Hodgkin lymphoma, post-bone marrow transplantation and after valproic acid treatment [4]. The anomaly in these clinical settings has been found together with various chromosomal aberrations, such as trisomy 18, t(5;17), t(7;17), del 17p i(17q), and $22p^+$ (5-8). The present case had Pelger-Hüet anomaly and t(4;21) in the bone marrow cells. Therefore, hereditary Pelger-Hüet anomaly, which is not usually associated with such chromosomal aberration, is unlikely. Moreover, the dysplastic morphological changes in the patient's bone marrow concur with the diagnosis. It is possible that the (4;21) translocation is etiologically associated with her disease, as well as with the Pelger-Hüet anomaly.

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Quantitative Analysis of MDR-1 Gene Expression in Acute Myeloid Leukemia by Reverse Transcription Polymerase Chain Reaction

To the Editor: Drug resistance is the main cause of treatment failure of acute myeloid leukemia (AML). Expression of the multidrug resistance (MDR) protein, P-glycoprotein 170 (P-gp), encoded by the MDR-1 gene, has been suggested as playing an important role in this mechanism. It was identified that the cancer cells acquired the capacity of increasing drug efflux through activating on energy-dependent membrance transport pump whose molecular basis is P-gp [1]. We used the reverse transcription polymerse chain reaction (RT-PCR) technique to investigate P-gp expression in AML. Twenty patients (female 10, male 10) with newly diagnosed AML were included in our study. Ages ranged from 20 to 82 years, with a median of 50 years, and the bone marrow (BM) aspirates were taken for cytological classification and AML phenotype according to the French-American-British (FAB) criteria. The proportion of leukemia blasts in their BM varied between 30% and 100%, with a median of 96%. After diagnosis, the chemotherapy was given on the protocol of the German AML Co-operative Group [2]. Twelve patients achieved subsequently complete remission (CR). The overall CR rate was 66%. The controls were provided by normal peripheral blood leukocytes from healthy volunteers, and by an MDR-negative Chinese hamster ovarian cell line and its colchicum-selected MDR variant (CHO-RT).

Total RNA (tRNA) was extracted with a guanidinium isothiocyanate buffer by phenol–chloroform and assessed spectrophotomertically. A five-carat cell cDNA was synthesized from 5 μg of tRNA using 100 ng of random hexadeoxynucleotide primer in 30 μl of a reaction solution at 37°C for 1 hr. PCR was performed with cDNA derived from 80 ng of RNA and reaction kits in a final volume of 25 μl. PCR conditions were: 94°C 45 secs, 60°C 1 min, 72°C 2 min, for a total of 40 cycles. *MDR-1* gene-specific sequences were amplified by using the sense-strand primer CCCATCATTG-CAATAGCAGG (residues 2596–2615) and the antisense-strand primer GTTCAAACTTCTGCT-CCTGA (residues 2733–2752), added at 37.5 pmol per reaction. PCR products were separated on 1.5% agarose gels and visualised by ultraviolet (UV) illumination. Several negative control reactions that contained water or cDNA reaction mixtures without RNA were included in each experiment.

Eighteen samples expressed *MDR-1* gene product, while other two suffering from biphenotypic AML were negative. The total *MDR-1* gene expression rate was 90%. P-gp expression did not correlate with age, sex, or FAB classification. By statistical analysis, the CR rate was not significantly different between patients with *MDR-1* gene expression and those without detectable expression. Eight of 8 patients without CR were *MDR-1* gene positive, while 10 of 12 patients with CR were positive as well. No significant correlation of *MDR-1* gene expression to other cell surface markers (CD2, CD13, CD14, CD19, CD33, TdT) was found. However, 7 of 8 nonresponders were positive for CD34, whereas 4 of 12 responders were positive (data not shown).

P-gp excludes drugs from the interior of cells to protect lymphocyte from toxic body product. Its distribution was thought to serve as a chloride ion channel, ATP channel, a membrane ATPase [1]. A recent report suggested that they may block drug or dye transport by efficiently competing for binding site on the transport pump or its cancer protein [3]. Our study demonstrated a fairly high incidence of *MDR-1* gene expression in AML, even those who never received any chemotherapy. However, no difference in the incidence of *MDR-1* gene expression between newly diagnosed patients and relapsed patients was found, as well no linear relationship between *MDR-1* gene expression and achievement of CR in patients with newly diagnosed AML or relapse. Hence, we cannot confirm that *MDR-1* gene expression could be used to predict the outcome of treatment of patients with AML [4]. The same observation has also been reported [5]. Interestingly, we found a higher level of CD34 to be a negative prognostic factor independent of *MDR-1* gene expression in AML. Therefore, many other molecular biological works, such as multidrug resistance associate protein (MRP), topoisomerase I and II, and glutathione, remain to be done before any firm conclusions can be drawn [4].

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Refractory Pancreatitis Associated With Graft-Versus-Host Disease in Fanconi Anemia

To the Editor: Fanconi anemia (FA) is an autosomal recessive disorder characterized by a high incidence of aplastic anemia, congenital malformations, and a constitutional chromosomal fragility syndrome [1]. Although the outcome of bone marrow transplantation (BMT) in FA patients has been improved by the use of decreased doses of cyclophosphamide (CY) as a preconditioning regimen, acute graft-versus-host disease (GVHD) is still the main cause of death after BMT in FA patients [2,3]. We present the susceptibility of the anomalous pancreas to GVHD in a FA patient after allogeneic BMT.

A 4-year-old girl with pancytopenia was referred to our hospital in 1993. Past history revealed only paleness of the patient over the previous years. Family history revealed two healthy siblings and healthy parents. Physical examination revealed short stature, microcephaly, skin pigmentation, and mental retardation. The remainder of the physical examination was normal.